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Dapivirine Ring Market Authorization Overview

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Market Authorization Overview

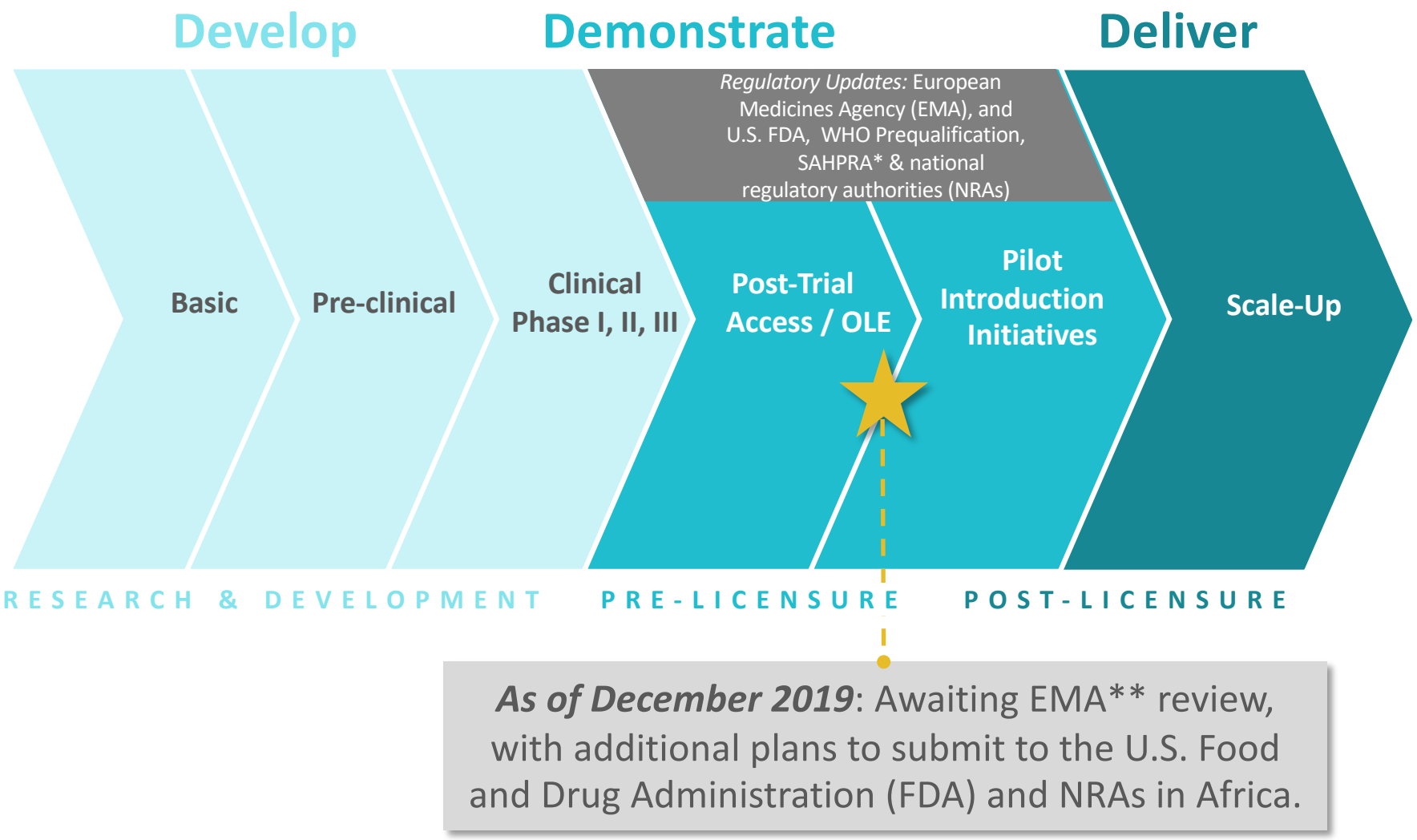
The following slides share a high-level picture of the necessary regulatory, normative guidance, and policy steps at the global and country levels to support introduction of the dapivirine ring.

The insights presented here are based on interviews and represent one possible path of market authorization. While it is likely that the ring pathway will follow many of these steps, it is also plausible that market authorization for the ring may chart a different path in some areas.

These insights are organized across two tracks and six steps, many of which can happen concurrently:

Global	National
Stringent Regulatory Authority (SRA) Approval	National Regulatory Authority (NRA) Approval
WHO Essential Medicines List (EML)	National Guidelines and Policies
WHO Prequalification (PQ)	
WHO Normative Guidance	

Where the Ring is today



As of December 2019: Awaiting EMA** review, with additional plans to submit to the U.S. Food and Drug Administration (FDA) and NRAs in Africa.

**South African Health Products Regulatory Authority*
***The European Medicines Agency*

Global market authorization activities

Stringent Regulatory Authority Approval

- Innovator products, such as the dapivirine ring, require approval from a stringent regulatory authority (SRA) like the FDA or EMA; most SRAs have similar levels of rigor.
  - USAID procurement policy generally requires SRA approval or WHO prequalification
  - Information included on a product label (e.g., indication, duration of use) of approved product by SRA / WHO PQ submissions can only be changed through resubmission procedure. If national regulatory authority (NRA) approval is granted with different product label, it is considered a different product that is no longer SRA approved / WHO prequalified.
- Dossiers submitted to SRAs follow the Common Technical Document (CTD) outline which divides the dossier into 5 modules – Module 1 contains country-specific information (administrative and prescribing information) and Modules 2 – 5 are specific to the product

WHO Essential Medicines List

- While the ring can receive WHO Prequalification without being on the WHO Essential Medicines List (EML), the usual practice is for a product to first be placed on the EML before beginning the WHO Prequalification process. The WHO EML is updated every 2 years.

WHO Prequalification

- WHO Collaborative Registration Procedure (CRP) may expedite NRA approval (separate GMP inspections are sometimes still required).
- In some instances, direct submission to NRAs may be faster – regulatory landscapes at the national level are constantly evolving.
- The WHO Prequalification Team for Medicines (PQTM) has been involved in the EMA review process for the ring.

WHO Normative Guidance

- A WHO program will develop normative guidance for the ring, which describe how the product should be used and delivered.
- The ring could be included in WHO normative guidance prior to WHO PQ.

National market authorization activities

National Regulatory Authority Approval

- The ring will require NRA approval in each country where the ring will be made available; most countries in sub-Saharan Africa will likely require an SRA approval prior to NRA approval, although they may accept approval by the South African regulatory agency.
- Dossiers for the ring submitted to NRAs of the 7 product launch countries* include the same Modules 2-5 of the SRA dossier, with an adapted Module 1 specific to the country.
- Most countries in the world require a local technical representative (LTR) to submit the dossier. LTR selection is important given their role in facilitating the approval process.
- Most countries do not require a local market authorization holder (MAH). If possible, the manufacturer should serve the role of MAH and not give up this control to a local entity.
- Many NRAs require their own good manufacturing practices (GMP) inspection of manufacturing facilities, even if the product is WHO Prequalified. Fees and time commitments for these inspections are substantial, but the processes are frequently evolving.

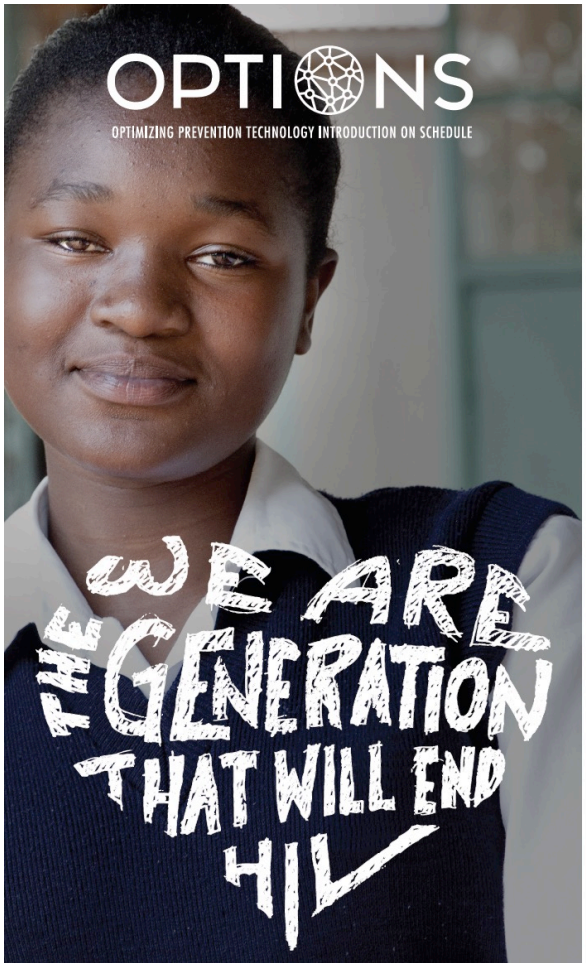
National Guidelines and Policies

- Most countries will rely on the WHO normative guidance and adapt it to the local country context.
- The process of guideline adoption for the ring will typically be led by a group such as the HIV prevention or PrEP technical working group (TWG), or another technical body.
- Some countries (e.g., Zimbabwe) have already included the ring in biomedical HIV prevention guidelines, but most will need to develop new guidelines for the ring.
- The WHO EML is also often adapted to a national EML.

*The seven countries involved in ring clinical trials: Kenya, Malawi, Rwanda, South Africa, Tanzania, Uganda, Zimbabwe

Appendix – Acronyms

CRP – Collaborative Registration Procedure
CTD – Common Technical Document
EMA – European Medicines Agency
EML – Essential Medicines List
FDA – United States Food and Drug Administration
GMP – Good Manufacturing Practices
OLE – Open Label Extension
LTR – Local Technical Representative
MAH – Market Authorization Holder
NRA – National Regulatory Authority
PQTM – Prequalification Team for Medicines
SAHPRA – South African Health Products Regulatory Authority
SRA – Stringent Regulatory Authority
TWG – Technical Working Group
USAID – United States Agency for International Development
WHO – World Health Organization



Thank you

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